Early Journal Content on JSTOR, Free to Anyone in the World

This article is one of nearly 500,000 scholarly works digitized and made freely available to everyone in the world by JSTOR.

Known as the Early Journal Content, this set of works include research articles, news, letters, and other writings published in more than 200 of the oldest leading academic journals. The works date from the mid-seventeenth to the early twentieth centuries.

We encourage people to read and share the Early Journal Content openly and to tell others that this resource exists. People may post this content online or redistribute in any way for non-commercial purposes.

Read more about Early Journal Content at http://about.jstor.org/participate-jstor/individuals/early-journal-content.

JSTOR is a digital library of academic journals, books, and primary source objects. JSTOR helps people discover, use, and build upon a wide range of content through a powerful research and teaching platform, and preserves this content for future generations. JSTOR is part of ITHAKA, a not-for-profit organization that also includes Ithaka S+R and Portico. For more information about JSTOR, please contact support@jstor.org.

FACTORS IN THE RESISTANCE OF GUINEA PIGS TO TUBERCULOSIS, WITH ESPECIAL REGARD TO INBREEDING AND HEREDITY

DR. SEWALL WRIGHT, S.D., AND DR. PAUL A. LEWIS, M.D.

BUREAU OF ANIMAL INDUSTRY, U. S. DEPARTMENT OF AGRICULTURE,
WASHINGTON, D. C., AND THE HENRY PHIPPS INSTITUTE, THE
UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA, PA.

IN the pre-bacteriologic era physicians were quite generally of the opinion that heredity played a large part in resistance or susceptibility to tuberculosis. Following Koch's demonstration of the part played by the *Bacillus tuberculosis* in the etiology of the disease it was recognized that the hereditary influences might be only apparent; the disease being established in any family there was evidently an immeasurably increased chance of interfamilial infection; and as a consequence of this uncertainty of interpretation it has become quite customary to regard hereditary influences, properly considered, as a negligible factor.

Pearson[1, 2] and Goring[3] compared the correlation between parent and offspring, in incidence of the disease, with that between husband and wife. The effects of unfavorable conditions and the chances of infection might be about as great in one case as in the other, while heredity would be a common factor only in the first case. Pearson dealt with upper class families of which one member was being treated in a certain sanitarium. The correlation between parent and offspring came out about .50, in the usual scale, in which 1.00 is perfect correla-

---

[1] Pearson, Karl, 1907, ''A First Study of the Statistics of Pulmonary Tuberculosis.'' Dulau & Co., London. 26 pages.

[2] Pearson, Karl, 1912, ''Tuberculosis, Heredity and Environment.'' Dulau & Co., London. 46 pages.

[3] Goring, Charles, 1909, ''On the Inheritance of the Diatheses of Phthisis and Insanity.'' Dulau & Co., London. 28 pages.

tion, after making certain assumptions in regard to the frequency of the disease in the whole population, and making allowance for the age of the children, many of whom had not reached the age of greatest danger. This correlation is about the same as that between parent and offspring in characters such as height, weight, eye color, etc., which are largely or wholly determined by heredity. The correlation between husband and wife was only .24 and even much of this, the author found reason for attributing to assortative marriage.

Goring's study was made with the families of British convicts. He also found a correlation of about .50 between parent and offspring but no correlation (— .01) between husband and wife. The only assumption that had to be made in this case was a correction for the age of the children.

We are acquainted with no experimental work bearing on this question.

Material

The present paper describes the results of experiments on certain inbred and crossbred stocks of guinea pigs. All of the animals used were a by-product of experiments on the effects of inbreeding which have been carried on by the Bureau of Animal Industry of the U. S. Department of Agriculture since 1906. One of the authors (Wright) has been in charge of these experiments since 1915. A detailed report on the results is soon to be published. A brief summary will suffice here.

Twenty-three families of guinea pigs were maintained for a number of years by mating exclusively brother with sister among the descendants of twenty-three original pairs. In sixteen cases (including families 2 and 13 of those tested for resistance to tuberculosis) both of the original parents came from a stock which had already been maintained for twelve years without the infusion of fresh blood, by the Experiment Station of the Bureau of Animal Industry. In the remaining families, including families 32, 35 and 39, the original females came from the above mentioned stock, while the original males were purchased from a local dealer.

In 1911 a number of animals were selected from the stock of the Experiment Station to start a control experiment. The mating of even second cousins has been avoided in this stock, which has been called Experiment *B*.

Eighteen of the inbred families were still on hand in 1916, having then on the average about eleven generations of brother-sister matings back of them. At this time most of the families were disposed of in order to make room for cross-breeding experiments and to obtain larger numbers from the five families which it was decided to retain. These families, numbers 2, 13, 32, 35 and 39, are the ones which have been tested for resistance to tuberculosis. They were retained in part because they already occupied many pens, but largely because of the possession of contrasting characteristics in size, fertility and coat pattern. Each of these families is at present very homogeneous in heredity. Family 2 is descended wholly from one mating in the sixth generation of inbreeding. Families 13, 32, 35 and 39 come from single matings in the seventh, eleventh, twelfth and eighth generations respectively.

The total number of animals involved in the experiment on inbreeding and cross-breeding has been about 30,000.

THE EFFECTS OF INBREEDING ON VIGOR

It is noteworthy that there has been no very obvious decline in vigor, although the families are now on the average in the fourteenth generation of brother-sister mating and one of the most vigorous (No. 35) has reached the twenty-first generation.

There has, however, been some decline in vigor in all respects which have been studied. The decline is most marked in fertility, including both frequency and size of litters. It has been so great in this respect that it would have to be recognized even though the decline in other respects were assumed to be due wholly to less favorable environmental conditions.

That there has been a real genetic decline in the inbred stock in all elements of vigor is shown by comparison with the control stock *B*, which has been superior in every respect. Still better evidence has been obtained by comparison of the inbreds with the young from crosses between the different families raised at the same time and under the same conditions.

The Effects of Crossing

In interpreting the effects of crossing, the characteristics which depend on the hereditary make-up of the young must be distinguished from those which depend on the dam or sire. In studying these questions, inbred females have been mated with inbred males of another family (experiment *CO*) and with crossbred males (experiment *CA*). Crossbred females have been mated with brothers (experiment *CI*), unrelated crossbred males (experiment *CC*) and inbred males of an unrelated family (experiment *AC*).

Size of litter appears to depend wholly on the dam. There is little or no improvement in the experiments in which the dam is inbred (*CO, CA*). There is, however, a marked increase, 10–30 per cent. depending on conditions, in the litters produced by crossbred females (*CI, CC, AC*).

The record of an experiment in frequency of litters depends on the age of maturity as well as on the regularity thereafter. Males mature considerably later than females, so that the age of maturity of the male is the controlling factor in this respect in matings, made as in the present experiments, between immature animals. The frequency of litters after maturity appears to depend largely on the dam. There is no improvement in the record of the first cross (*CO*) over the inbreds. There is, however, marked improvement in the other experiments in which either the sire or dam or both are crossbred. Crossbred males mature earlier and the crossbred females have litters more regularly than inbreds.

The percentage of the young born alive depends almost wholly on the dam. There is little or no improvement in experiments *CO* and *CA*, but an increase of 6 to 8 per cent. where the dam is crossbred. The percentage which are raised to 33 days of age of the young born alive depends both on the dam and on the heredity of the young. There is a marked increase, 9 to 12 per cent., in all of the crossbreeding experiments mentioned above.

Somewhat similarly, birthweight depends largely on the dam, while the gains between birth and 33 days depend to a considerable extent, though far from wholly, on the heredity of the young. Guinea pigs become independent of the dam at a very early age. There is an increase of 2 or 3 per cent. in experiments *CO* and *CA*, but one of about 7 to 10 per cent. where the dam as well as the young are crossbred. In the gain between birth and 33 days, there is an improvement of about 16 per cent. in the first cross, which is somewhat increased in the young produced by crossbred dams. There is an increase of 15 to 20 per cent. in the adult weight in the first cross (*CO*). This is maintained in the young produced by matings of unrelated crossbreds (*CC*), but half of it is lost where the parents, though crossbred, are brother and sister (*CI*). The influence of the dam does not appear to extend to the adult weight.

A loss in the improvement brought about by the crossing becomes apparent in the second generation of inbreeding following a cross (experiment *C*2) in those cases in which it is not apparent in the first generation.

COMPARISON OF DIFFERENT FAMILIES

A comparison of the different inbred families with each other has revealed persistent differences in color, pattern, tendency toward polydactylism, tendency toward production of monsters, mortality among the young, weight and both elements of fertility. It was found that the differences in these respects could not be interpreted merely as differences in general vigor. Vigor above the average in one respect was as likely as not to be found associated with a subnormal record in another respect, the correlation between the records of the families in two respects coming out in most cases substantially zero. Examples of these family differences will be brought out later in connection with the effects of inoculation with tuberculosis.

EXPLANATION OF THE RESULTS OF INBREEDING AND CROSSING

These results harmonize well, on the whole, with those found by other investigators. It is believed that they can be explained as consequences of the current theory of heredity without recourse to the rather mystical ideals which once prevailed in regard to inbreeding. There appear to be independently inherited factors which affect frequency and size of litter, ability to bear the young successfully, vitality and growth as well as for color, pattern and the other characters in which the families differ. There seem to be surprisingly few factors which act on all of these characteristics. The concept, hereditary vigor, thus becomes merely an expression for the sum of a number of independently inherited qualities and not an entity.

The factors which cause reduced vigor in any respect appear to be in general recessive. The primary effect of inbreeding is to render homozygous a random group of the factors present in the original stock. Some combination of factors, good, bad and indifferent, thus becomes fixed in each inbred line. As the recessive factors, tending toward lack of vigor, are as likely to become fixed as the dominant ones there is on the average a decline in vigor in each respect. Moreover, owing to the likelihood that many factors for vigor will be linked genetically with factors causing weakness, it is to be expected that vigor in all respects will be found in very few lines, even where there is careful selection. In the present case, there was very little conscious selection but a considerable amount of natural selection was, of course, unavoidable.

On crossing two inbred lines, each, as a rule, supplies some of the dominant factors lacking in the other, with the consequence that there is increased vigor in so far as the character in question depends on the heredity of the animal itself. In the next generation if brother-sister matings are made, there should be a decline as compared with the first generation in characters which depend wholly on the animal itself. The decline from this cause may, however, be balanced or more than balanced by the improvement due to the influence of the crossbred dam.

EXPERIMENTS ON RESISTANCE TO TUBERCULOSIS

Since April, 1919, all surplus individuals in five inbred families (2, 13, 32, 35 and 39) and a random selection from certain crossbreeding experiments (*CO, CA, AC,* and *B*) have been shipped from Washington to Philadelphia to be tested for resistance to tuberculosis. The animals were shipped in lots of 30 to 60 every two or three weeks. They were from 5 to 8 weeks old at the time of shipping. They usually arrived in good condition but with some loss in weight. The first two lots were not tested because of heavy mortality before inoculation due to feed conditions. Lot 6 was not tested because of heavy mortality due to excessive heat during shipment. Data on the shipment and inoculation are presented in Table I. The deaths within 15 days after inoculation are probably not attributable to tuberculosis and are not considered in the later work. The experiments were considered closed when all but two or three of the animals had died. The last column gives the number of days after inoculation at this time. The next to the last column gives the day by which 50 per cent. of those which passed 15 days had died. It agrees fairly well with the average number of days calculated on the assumption that the few survivors of the experiment died on the day following that given in the last column.

The cultures used were of the human type of tuberculosis with the exception of lot 3 in which the type was bovine.

TABLE I

Lot	Date Shipped	Date Inoculated	Inoculation	No. Died Before 15 Days	No. Survived 15 Days	Av. No. of Days Lived	Day to which 50 % Survived	Day Exp. Closed
3	May 4	June 2, 1919	1/10 mg. culture 07.8 intraperitoneal	2	32	43.9	44	62
4	June 4	" 10, "	1/5 " 465 "	5	30	25.9	21	40
5	" 18	July 3, "	1/10 " 465 "	7	57	24.0	24	31
7	July 17	Aug. 25 "	1/5 " DG "	3	37	25.6	24	43
8	" 30	" "	" " " "	1	28	25.2	24	38
9	Aug. 14	" "	" " " "	3	44	25.3	24	39
10	" 28	Oct. 24 "	" " " subcutaneous	6	46	49.7	47	84
11	Sept. 11	" 25 "	" " " "	3	31	54.2	54	83
12	" 25	" " "	" " " "	2	30	49.5	46	83
13	Oct. 9	" " "	" " " "	3	42	45.2	40	83
14	" 23	" " "	" " " "	2	35	42.3	39	83

Lots 7, 8 and 9 were given the same inoculation on the same day. The results are so similar, in spite of the differences in the age and weight of the animals, that they can be dealt with satisfactorily as one experiment. Lots 10 to 14 were all given the same inoculation on October 24 and 25 and can also be dealt with as one experiment. The same quantity of the culture, inoculated intraperitoneally in lots 7 to 9, was inoculated subcutaneously in lots 10 to 14, with the consequence that the average length of life was much greater in the latter group of lots. Lots 3, 4, and 5 were inoculated separately with different cultures or different amounts of the same culture. The numbers in each case are rather small for separate treatment. The mortality curves for lots 4 and 5 are not, however, very different. That for lot 3 can be made similar by multiplying the days of survival after inoculation by 3/5. These three lots have been combined in this way for comparison with the later and more satisfactory experiments.

SEX AS A FACTOR IN RESISTANCE

In attempting to analyze the difference in the length of life following inoculation, we will consider first a number of possible factors other than heredity. It will be convenient to start with sex. Chart 1 shows the percentage of the males and females alive at the beginning of each day in lots 10 to 14, starting with 100 per cent. on the fifteenth day after inoculation. The males have some advantage in lots 10–14, but it is too small to be of more than doubtful significance. In lots 3 to 9, moreover, the two mortality curves keep crossing each other in such a way as to indicate that sex makes no appreciable difference in resistance.

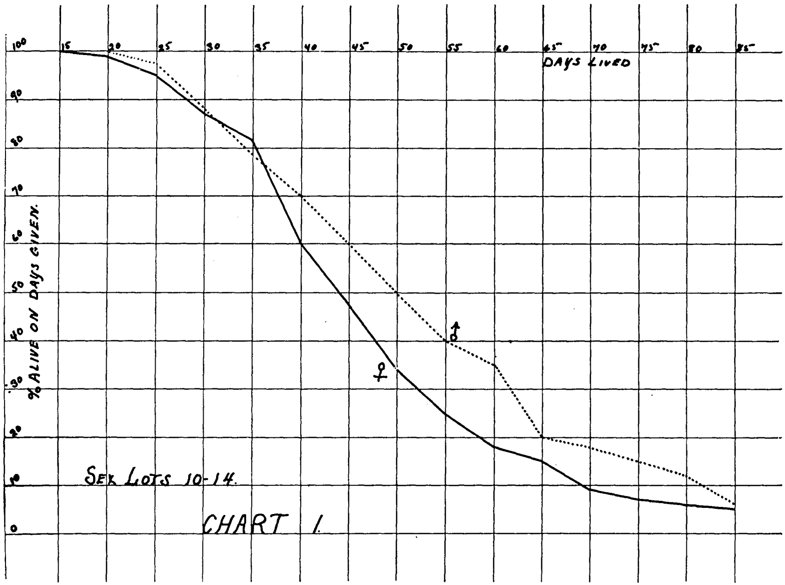

CHART 1. The mortality curves of the males and females of lots 10 to 14. This and the later charts give the percentage alive at the beginning of each five-day period starting with 100 per cent. on the fifteenth day after inoculation.

THE AGE OF THE DAM AS A FACTOR

Some rather dubious indications of a relation between age of mother and susceptibility of the offspring to tuberculosis were found by Pearson among human beings.

The guinea pigs in lots 10–14 were divided into two groups, those containing at least 25 per cent. of the blood of family 35 and the remainder. Each of these groups was classified by birth rank with results given in Table II.

TABLE II

AVERAGE NUMBER OF DAYS SURVIVAL AFTER INOCULATION AMONG THE YOUNG IN DIFFERENT BIRTH RANKS, LOTS 10–14

Order of Litter	Animals with Blood of Family		Miscellaneous	
	No.	Av.	No.	Av.
1	16	58.9	17	35.6
2	21	60.3	29	43.1
3	7	70.6	23	43.3
4	12	63.3	26	39.8
5	4	60.8	6	35.8
6			11	45.9
7			5	37.1
8			3	33.3
8 +			4	30.8

These figures suggest an increase in resistance of the young born in litters up to the third and a decline in resistance in young born of aged dams. They must be confirmed by larger numbers, however, before much significance can be attached to them.

THE RELATION OF AGE, WEIGHT AND RATE OF GAIN TO RESISTANCE

Mere bulk must be considered as likely to be a factor in resistance to tuberculosis. Other things being equal, one would expect to find that the same inoculation given to a St. Bernard and to a toy spaniel would have a more disastrous effect on the latter. In lots 10–14, some of the guinea pigs were over three times as heavy as others at the time of inoculation (variations between 120 and 440 grams).

The rate of gain is a good indication of the condition of the animals and is thus another factor which one would expect to find correlated with resistance to disease. In this connection, we have for study the birth-weight, weight at 33 days and the rate of gain between 33 days and inoculation. The birthweight varies between 40 and 120 grams, the weight at 33 days between 90 and 360 grams, and as to rate of gain after 33 days, some lost weight while others gained over 3 grams a day.

Age is a factor which must be considered apart from weight and rate of gain. In lots 10–14, there were variations between 35 and 105 days at the time of inoculation. In lots 7–9 the variation was between 45 and 85 days.

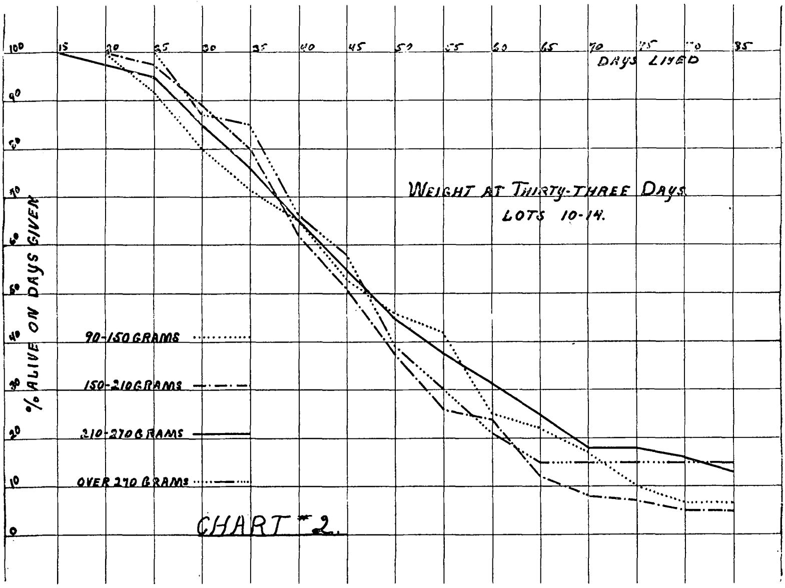

Chart 2. The mortality curves of the guinea-pigs of lots 10–14, grouped according to weight at weaning.

The correlation between the length of life after inoculation and each of these factors, including also size of litter, is given in Table III for lots 7–9 and lots 10–14. All of these correlations were calculated by the usual product

TABLE III

Factors Correlated	Lots 7, 8, 9	Lots 10-14
Days lived—Size of litter	+ .090 ± .064	+ .029 ± .050
—Birth weight	— .044 ± .064	+ .059 ± .050
—Weight at 33 days	+ .022 ± .065	+ .056 ± .050
—Rate of gain (33-inoc.)	+ .120 ± .064	+ .223 ± .047
—Age at inoculation	+ .025 ± .065	+ .180 ± .048
—Weight at inoculation	+ .092 ± .064	+ .219 ± .047

moment method. Perfect positive correlation is + 1, perfect negative correlation is *— 1, while 0 indicates the* absence of correlation.

Inspection of these figures reveals that all of them are surprisingly low. In lots 7–9, the factor most closely correlated with length of life is the rate of gain between weaning (33 days) and inoculation, and even this is not certainly significant in view of its probable error (+ .120 ± .064). Larger correlations are to be expected in lots 10–14, owing to the greater heterogeneity in age and weight, but even here the correlations are all small. Size of litter, birthweight and weight at 33 days are again of no value as indicators of resistance to tuberculosis. There, are, however, significant correlations between length of life and rate of gain (+ .223 ± .047), age (+ .180 ± .048) and weight of inoculation (+ .219 ± .047).

The degree to which variation is determined by a given factor is measured by the square of the coefficient of correlation. On this basis, only 5 per cent. of the variation in length of life (*i.e.*, 5 per cent. of its mean square deviation) is determined by the most important of the above factors. The degree of determination by all of these factors combined can not be found by merely adding the squares of the correlations, because the factors are not independent of each other. For example, rate of gain is an element in determining the weight at inoculation. Any effect which it has on resistance should be reflected in a correlation between weight and length of life as well as between rate of gain and length of life. The correlations among the more important of these factors are given in Table IV.

TABLE IV

		Lots 7, 8, 9	Lots 10–14
Weight at inoculation	—Rate of gain	+ .357 ± .056	+ .553 ± .035
	—Age	+ .420 ± .054	+ .742 ± .022
	—Weight at 33 days.	+ .780 ± .025	+ .670 ± .027
Rate of gain	—Age	+ .323 ± .058	+ .592 ± .032
	—Weight at 33 days.	— .153 ± .063	— .040 ± .050
Weight at 33 days	—Age	— .012 ± .065	+ .160 ± .048

Weight at inoculation is of course completely determined by the weight at 33 days and the rate of gain and age at inoculation. The correlations between weight at inoculation and these three factors are accordingly high. They are rather different in the two groups of experiments, but this is to be expected. There was much less variation in age in lots 7–9 than in lots 10–14 and variation in age accordingly plays a less important part in determining the variations in weight than in the latter case. The rather high correlation between age and rate of gain is due to the fact that nearly all of the guinea pigs suffered a loss in weight following shipment at a little over 33 days of age. Thus the older they were at inoculation, the greater the time in which they had to recover from the effects of shipping. The rate of gain before 33 days is generally an indication of the probable later rate of growth. In the present case, however, the slight negative correlation between the rates of gain before and after 33 days seems to indicate that shipping delayed

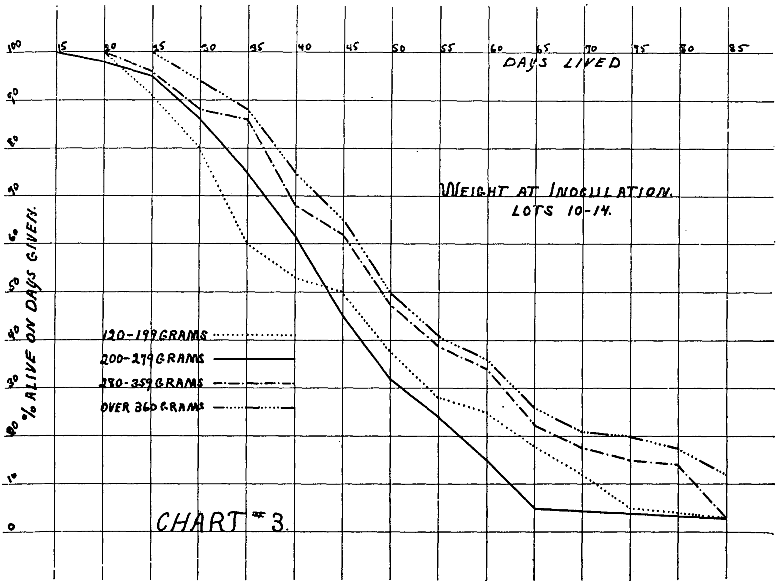

CHART 3. The mortality curves of the guinea-pigs of lots 10–14, grouped according to weight at inoculation.

more the growth of those guinea pigs which had been gaining rapidly than of those which had more growth to make up. The small positive correlation between weight at 33 days and age at inoculation reflects a decline in the condition of the stock, due probably to the use of an inferior quality of hay, which took place during the summer of 1919, especially during the time in which lots 10–14 were being raised.

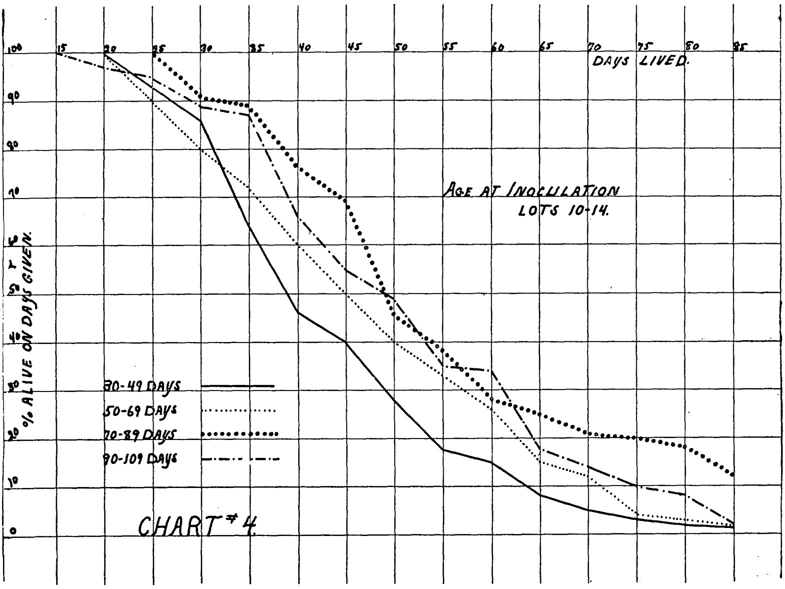

CHART 4. The mortality curves of the guinea-pigs of lots 10–14, grouped according to age at inoculation.

With the help of these correlations, we can calculate the degree to which variation in length of life is determined by each factor separately and by all of them combined. For the last purpose, Pearson's coefficient of multiple correlation can be used. This coefficient comes out +.136 in lots 7–9 and +.251 in lots 10–14 for the correlation between length of life and rate of gain after 33 days, age and weight at inoculation combined. The degree of determination is measured by the square of this coefficient. These three most important factors combined, therefore, determine less than 2 per cent. of the variation in length of life in lots 7–9 and less than 7 per cent. in lots 10–14. The separate contributions of the various factors can be calculated with results given in the following table.

TABLE V

DEGREE OF DETERMINATION OF DAYS LIVED AFTER INOCULATIION BY AGE, WEIGHT AND RATE OF GAIN

Factors	Lots 7–9	Lots 10–14
Direct effect of age	.0015	.0005
weight	.0049	.0229
rate of gain	.0116	.0233
age and weight	—.0023	—.0051
age and rate of gain	—.0027	—.0041
weight and rate of gain	+ .0054	+ .0256
Total degree of determination	.0184	.0631

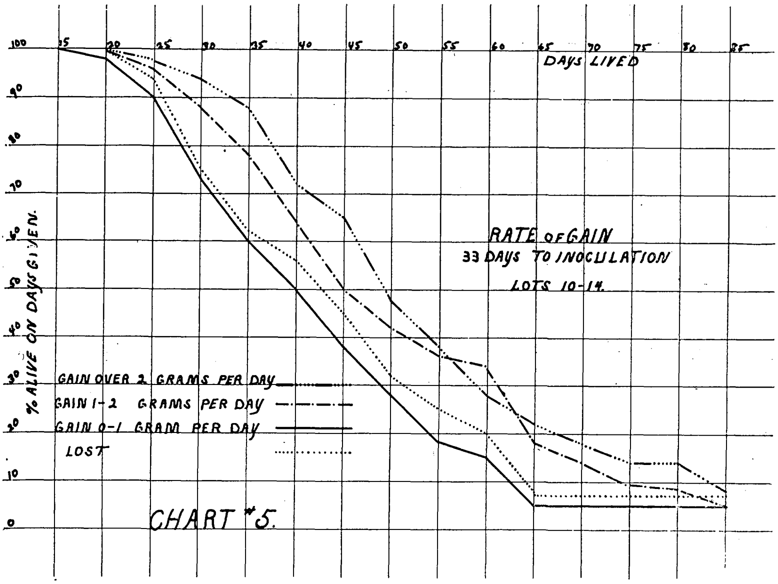

CHART 5. The mortality curves of the guinea-pigs of lots 10–14, grouped according to the rate of gain between weaning and inoculation.

While these figures can not be trusted in detail, owing to the large size of the probable errors of the correlations on which they are based, they indicate that age within the limits of one to three months has virtually no direct effect whatever on resistance to tuberculosis. There seems to be a slight direct effect of absolute weight and a slightly greater direct effect of rate of gain, presumably as a measure of the condition of health.

NOTE

It may be of interest to readers who are not familiar with this method of analysis to compare the degrees of determination shown in Table V with those in a case in which we know a priori that there is complete determination of one variable by a number of others. The data for such a case have already been presented. The weight at inoculation is completely determined by weight at 33 days and the product of the rate of gain and interval between 33 days and inoculation. The coefficient of multiple correlation between weight at inoculation and these three factors combined comes out .9884 in lots 7–9 and .9628 in lots 10–14. The degrees of determination are as follows:

TABLE VI

Factors	Lots 7–9	Lots 10–14
Direct effect of weight at 33 days	.7106	.3689
rate of gain	.1501	.0907
age	.0930	.2177
Joint effect of weight at 33 days and rate of gain.	—.0500	—.0073
weight at 33 days and age	—.0031	.0907
rate of gain and age	.0763	.1663
	.9769	.9270

The departure of the multiple correlations and the sums of the degrees of determination from unity are of the order usually met in such cases. This method of analysis applies strictly only where the effects of the factors are combined by addition and the correlations are linear, conditions which are not perfectly met in the present case.

The facts brought out by the method of correlation are presented graphically in Charts 2, 3, 4 and 5. These charts show the decline in numbers, on the basis of 100 per cent. alive on the 15th day after inoculation among groups of guinea pigs of lots 10–14, classified by weight at 33 days, weight at inoculation, and rate of gain.

As a result of the foregoing considerations, it must be concluded that the apparent condition of a guinea pig at the time of inoculation and a knowledge of its past history give exceedingly little indication as to its probable length of life after inoculation. Over 98 per cent. of the variation in length of life in lots 7–9 and over 93 per cent. in lots 10–14 is caused by factors other than those discussed. This leads us to a consideration of hereditary differences as one of the possible causes of this variation.

HEREDITARY DIFFERENCES IN RESISTANCE

The average length of life in each inbred family and crossbreeding experiment in lots 3–5, 7–9 and 10–14 is given in Tables VII. VIII and IX together with other data. The distribution of the deaths is given in Tables X, XI and XII. As already stated, most of the lots were brought to a close while a few animals were still living. This introduces an element of uncertainty into the aver-

TABLE VII

AVERAGES OF THE CHARACTERISTICS OF THE GUINEA PIGS TESTED FOR RESISTANCE TO TUBERCULOSIS IN LOTS 3, 4 AND 5.

The days lived in lot 3 are multiplied by 3/5 to make the average about the same as in lots 4 and 5.

Family or Experiment	Number Tested	Size of Litter	Birth Weight	Wt. at 33 Days	Wt. at Inoculation	Age at Inoculation	Av. Days Lived
2	28	2.85	73.3	201.1	209.8	54.6	23.1
13	15	3.13	83.4	232.7	227.7	49.7	20.3
32	2	2.50	80.5	256.0	215.0	53.0	21.0
35	9	2.56	86.5	252.0	236.7	50.5	25.7
39	1	4.00	77.0	157.0	140.0	49.0	16.0
CO	10	2.70	82.1	236.5	243.5	51.5	26.0
CA	24	3.08	85.5	247.4	247.7	52.0	25.7
AC	21	3.76	77.8	230.2	223.6	51.3	27.4
B	9	2.33	101.2	277.9	280.6	54.2	25.8
Inbred	55	2.89	78.5	219.2	218.0	52.4	22.6
Crossbred	64	3.14	84.6	244.4	243.7	52.0	26.3

TABLE VIII

AVERAGES OF THE CHARACTERISTICS OF THE GUINEA PIGS TESTED FOR RESISTANCE TO TUBERCULOSIS IN LOTS 7, 8 AND 9

Lots 7, 8, 9	No.	Size of Litter	Birth Weight	Weight at 33 Days	Weight at Inoculation	Age at Inoculation	Av. Days Lived
2	13	2.46	80.2	197.1	243.1	64.2	22.8
13	16	2.81	91.0	257.1	308.1	63.6	23.9
32	10	2.40	86.6	224.4	273.0	71.8	20.6
35	9	2.56	85.0	242.5	282.2	61.2	27.1
CO	13	3.00	80.2	226.2	286.2	67.8	31.5
CA	14	2.93	80.1	213.1	251.4	58.1	24.0
AC	21	3.38	74.6	213.0	257.6	61.9	25.6
B	13	3.38	83.7	249.5	320.0	69.2	24.8
Inbred	48	2.58	86.0	231.3	278.3	65.0	23.5
Crossbred	61	3.20	79.0	223.6	275.6	63.8	26.8

ages, but the assumption that these survivors died on the following day is unfair only to the superior stocks.

TABLE IX

AVERAGES OF THE CHARACTERISTICS OF THE GUINEA PIGS TESTED FOR RESISTANCE TO TUBERCULOSIS IN LOTS 10–14

Lots 10–14	No.	Size of Litter	Birth Weight	Weight at 33 Days	Weight at Inoculation	Age at Inoculation	Days Lived
2...........	27	2.56	73.1	175.0	254.4	76.9	45.3
13...........	18	2.67	84.2	221.1	301.1	91.3	35.7
32...........	5	2.20	88.0	223.2	228.0	63.0	35.4
35...........	22	2.73	83.8	231.6	301.4	72.8	58.5
CO..........	26	2.81	82.8	210.9	274.6	66.8	52.7
CA..........	33	3.45	72.3	195.6	274.8	69.8	56.5
AC..........	31	3.26	75.3	213.7	273.9	68.1	45.9
B...........	22	3.09	79.5	220.1	280.9	67.7	40.0
Inbred.......	72	2.61	80.2	207.2	278.6	73.3	46.2
Crossbred....	112	3.18	77.0	209.0	275.7	68.2	49.4

TABLE X

THE NUMBER OF DAYS FROM INOCULATION TO DEATH IN EACH EXPERIMENT IN LOTS 3, 4 AND 5

The intervals in lot 3 are multiplied by 3/5 to make them equal on the average to those in lots 4 and 5. The deaths before 15 days are given in Table I. The animals in experiments *CO, CA* and *AC* are also classified by the amount of blood of family 35 at the bottom of the table. The last column includes two animals in lot 3 which survived at 61 days, one in lot 4 which survived at 42 days, and 3 in lot 5 which survived at 30 days.

	Experiment																	
	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	30+	Total
2....	1	2	1			4	5		2	1	2	1	2	5	2			28
13....			2		2	3	5	1	2									15
32....						1		1										2
35....					1			2		1			1	1	2		1	9
39....		1																1
B.....						1	1	1			2	2		1			1	9
CO...							1	2	1	1	3						2	10
CA...				1	3	1	3	1		1	1	1	2	2	3		5	24
AC...					2	1	1			1	1	4	1	3	2		5	21
0 (35).					5	2	5	1	1	3	5	2	1	3	3		6	37
$\frac{1}{4}$ (35).								1				1	1	1	1		1	6
$\frac{1}{2}$ (35).				1				1				2	1	1	1		5	12

THE EFFECT OF INBREEDING

In each case, the crossbreds (*CO, CA,* and *B*) lived a little longer on the average than the combined inbred families. This result is in line with the results of cross-

TABLE XI

THE NUMBER OF DAYS FROM INOCULATION TO DEATH IN EACH EXPERIMENT IN LOTS 7, 8 AND 9

	Experiment																											
	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	4o	41	42	42 +	Total
2		3	1		1		3	2	2											1								13
13				1	2	4	1	4		2				1	1													16
32	1	1	2	2	1			3																				10
35						1		2	3						1	1				1								9
B						1	1	5	4	1																1		13
CO							3		2		1				1		1					2	1			1	1	13
CA						2	3	2	7																			14
AC			1	2	2	3	2	3	1				1	1	2		1			1		1						21
0 (35)			1	2		4	6	1	5		1		1		2		1											24
$\frac{1}{4}$ (35)					1	1	2	2	2					1	1													10
$\frac{1}{2}$ (35)					1			2	3								1			1		3	1			1	1	14

TABLE XII

THE NUMBER OF DAYS FROM INOCULATION TO DEATH IN EACH EXPERIMENT IN LOTS 10 TO 14

	Experiment															
	15	20	25	30	35	40	45	50	55	60	65	70	75	80	82+	Total
2		3	3	2	4	3	2	1	2	3	1	1	1	1		27
13			4	6	4	1	1	1	1							18
32	1			1	1	1	1									5
35				1	3	2	2	2	2	2	1	1	1	2	3	22
B		1	4	1	6	4	2	2	1	1						22
CO		1	1	1	3	3	3	3	3	2	1	2			3	26
CA				2	2	1	6	4	3	8	2		1	2	2	33
AC		2	4	2	4	3	6	3		2	2			2	1	31
0 (35)		3	5	4	8	5	10	6	4	6					1	52
$\frac{1}{4}$ (35)				1	1	1	3	1	1	1	1			1	2	13
$\frac{1}{2}$ (35)						1	2	3	1	5	4	2	1	3	3	25

ing on vigor in other respects. In the present case, however, the difference does not appear very striking. In particular, the superiority of the control stock *B* over the inbreds seems very dubious. An earlier test of this question was made by Mr. E. H. Riley and Dr. E. C. Schroeder, of the Bureau of Animal Industry, when the inbred stock was in the sixth and seventh generations of inbreeding. They found that the inbred was distinctly inferior to the control stock in resistance. At that time, however, eighteen families were on hand. It is not unlikely that the four families tested in the present experiment are a selected lot in respect to resistance.

Returning to Tables VII, VIII and IX, there are no differences between experiments *CO* (parents unrelated inbreds), *CA* (sire crossbred, dam inbred) and *AC* (sire inbred, dam crossbred), which indicate an influence of the breeding of the dam on the resistance of the young. There are rather large differences, it is true, but these are not consistent and must be attributed largely to heredity from particular families rather than to the system of breeding.

DIFFERENCES IN RESISTANCE AMONG INBRED FAMILIES

Passing now to a comparison of the different inbred families with each other, we come to results which appear much more striking than the differences between inbreds and crossbreds. In all three groups of experiments, one family, 35, stands out as distinctly more resistant than the others. It leads the average of the others by 16 per cent. in lots 3–5, 19 per cent. in lots 7–9 and 43 per cent. in lots 10–14. The more striking result in the last case is probably due to the weaker inoculation. In spite of the large amount of variation in each case, the probable errors put the superiority of Family 35 beyond question. Among the other families, family 2 is on the whole the most resistant. Families 13 and 32 are about equally susceptible. Only one animal from family 39 was tested. This one was one of the first in its lot, no. 7, to die, indicating low resistance in this family also so far as conclusions can be based on such a slender basis.

INHERITANCE OF RESISTANCE AMONG CROSSBREDS

If there are hereditary differences in resistance, one might expect to find differences among the crossbreds depending on the families which went into their ancestry. A preliminary test of this point was made as follows: The length of life of each crossbred (*CO*, *CA* or *AC*) was entered under each of the four grandparental inbred families. Thus an animal in experiment *CA*, whose sire was a cross between families 35 and 2 and whose dam was of family 13, was entered once under each of the former families and twice under family 13. The averages of the entries under each family in this tabulation are given in Table XIII. It will be seen that in each group of experiments, family 35 has a distinct lead over the others as ancestral to resistant crossbreds. Family 39 and the other families which entered into the ancestry of the crossbreds appear to rank with the more susceptible families 13 to 32. It will be seen that the rank of families 35, 2, 13 and 32 as ancestors of resistant crossbreds is the same as their own rank in resistance. These results are brought out more clearly in a tabulation in which all of the crossbreds are classified as half-blood, quarter-blood and zero-blood of family 35. The last class may be divided into half-blood, quarter-blood and zero-blood of family 2. The results in comparison with those for family 35, 2 and the others combined are given in table XIV.

TABLE XIII

AVERAGE NUMBER OF DAYS LIVED BY THE CROSSBREDS DESCENDED FROM EACH INBRED FAMILY

Each crossbred is entered under the family of each grandparent.

Family	Lots 3, 4, 5		Lots 7, 8, 9		Lots 10–14	
	No.	Av.	No.	Av.	No.	Av.
35	30	27.9	38	30.3	63	64.4
2	65	25.9	56	26.8	116	51.4
13	45	24.8	49	26.0	72	48.7
32	33	24.4	21	23.9	51	49.0
39	28	26.0	16	24.9	39	48.0
Misc.	19	26.0	12	24.2	19	48.8

The half-bloods of family 35 are distinctly superior to family 35 itself, and thus much superior to their other ancestral families.[4] In the three groups of experiments

---

[4] The preliminary study of another large series of animals (lots 15 to 21) shows that while the order among the crossbreds, as related to the presence of the blood of family 35 has been maintained, the advantage of the half-bloods over family 35 is absent, the curves being almost the same with the half-bloods slightly less. The order of the inbred families it may be added remains exactly as described.

TABLE XIV

The Average Number of Days Lived by the Crossbreds which are ½ Blood, ¼ Blood and have no Blood of Family 35, the Last Class being Classified Similarly with Respect to Family 2

The averages for Families 35, 2 and the other inbred families combined are given for comparison.

	Lots 3, 4, 5		Lots 7, 8, 9		Lots 10–14	
	No.	Av.	No.	Av.	No.	Av.
½ blood (35)	12	28.9	14	32.2	25	65.6
¼ blood (35)	6	28.7	10	24.8	13	56.5
No blood (35)	37	25.0	24	24.4	52	43.9
No (½ blood 2)	16	25.9	11	24.4	32	46.0
blood (¼ blood 2)	16	24.4	10	24.0	13	39.2
(35) (No blood 2)	5	23.8	3	25.7	7	43.6
Family (35)	9	25.7	9	27.1	22	58.5
Family (2)	28	23.1	13	22.8	27	45.3
Other Inbreds	18	20.4	26	22.6	23	35.6

3–5, 7–9 and 10–14, these half bloods exceed family 35 by 13 per cent., 19 per cent. and 12 per cent. respectively in duration of life, and exceed the other inbred families by 31 per cent., 42 per cent. and 60 per cent. respectively. We have here more decisive evidence of the improvement in vigor in this respect which may follow a cross, than in the comparison previously made between the total inbreds and total crossbreds. The most probable explanation is the same as that applied to the improvement in fertility, weight and death rate following crosses, viz., that each inbred family tends to supply dominant factors, favoring vigor, which are lacking in the other. Applied to the present case, this means not only that family 35 possesses dominant factors for resistance, lacking in the other families, but that some or all of the latter may possess such factors lacking in family 35. By inbreeding among the crossbreds, it should be possible to develop a strain even more resistant than family 35 provided that the linkage relations do not interfere with the fixation of the factors for resistance in one strain.

The quarter-bloods of family 35 confirm the conclusions derived from consideration of the half bloods. They are about intermediate between the half-bloods

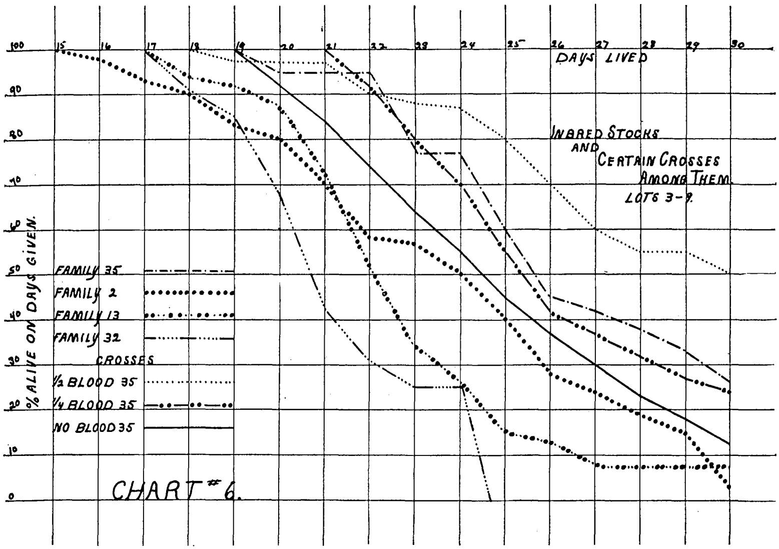

Chart 6. The mortality curves of the guinea-pigs of lots 3-9, grouped by breeding. Four inbred families. The crossbreds are grouped according to the amount of blood of the most resistant inbred family, No. 35.

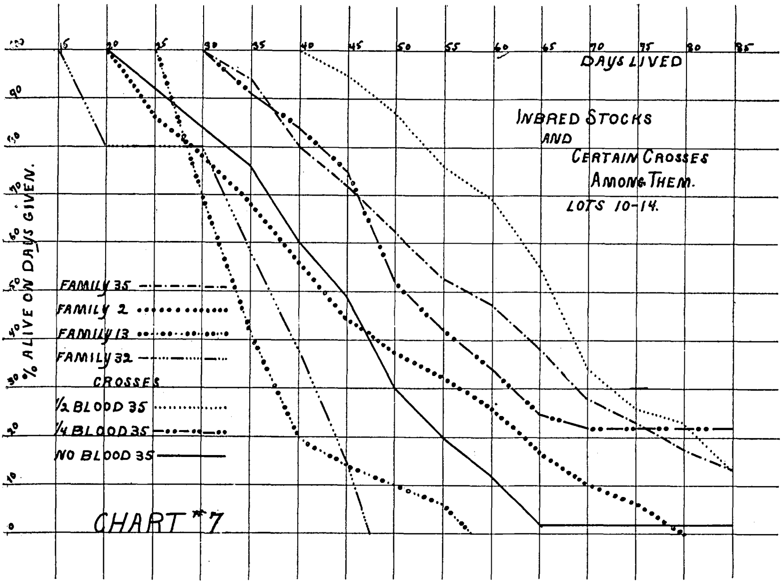

Chart 7. The mortality curves of the guinea-pigs of lots 10-14, grouped by breeding as in Chart 6.

and zero-bloods in lots 10–14 and in a combination of lots 3, 4, 5 with lots 7, 8, 9.

Curiously enough the crossbreds with no blood of family 35 do not show the improvement over their ancestral inbred families shown by the half and quarter bloods. They exceed the average of families 2, 13 and 32 by only 13 per cent. in lots 3–5, 8 per cent. in lots 7–9 and 7 per cent. in lots 10–14. They are not consistently superior to the best of these families, family 2. There seems to be dominance of resistance on the whole but no supplying of complementary factors for resistance such as was indicated in the crosses of family 35. This indicates that families 2, 13 and 32 are in the main susceptible because of the same genetic factors. The relations of the factors present in the different families is a question on which it is hoped more extensive evidence can be presented later (Charts 6 and 7).

INHERITANCE OF RESISTANCE AND SEX

The crosses involving family 35 give some evidence on the inheritance of resistance from sire and dam. The average length of life in reciprocal crosses is given in Table XV.

TABLE XV

THE AVERAGE LENGTH OF LIFE OF MALES AND FEMALES FROM RECIPROCAL CROSSES INVOLVING FAMILY 35

	No.	Av. Days
♂ (35) × ♀ (misc.)	7♂	63.6
	5♀	59.4
	12	61.9
♂ (35 × misc.) × ♀ (misc.)	6	64.0
Total, (35) on sire's side	18	62.6
	No.	Av. Days
♂ (misc.) × ♀ (35)	7♂	73.6
	6♀	63.7
	13	69.0
♂ (misc.) × ♀ (35 × misc.)	7	50.1
Total, (35) on dam's side	20	62.4

The results are irregular, as might be expected with such small numbers, but they show that there is transmission of resistance from each parent to offspring of each sex. The total figures—62.6 days where family 35 is on the sire's side, 62.4 where on the dam's side—indicate that there is probably equal inheritance from each sex.

DEGREE OF DETERMINATION OF RESISTANCE BY HEREDITY

We have shown that the length of life after inoculation was determined less than 2 per cent, by weight, age and rate of gain combined, in lots 7–9 and less than 7 per cent. by these factors in lots 10–14. It is interesting to compare the degree of determination by heredity with these figures. Such a comparison can be made for the crossbreds by finding the correlation between length of life and the amount of blood of family 35. The correlation in lots 3–5 comes out $+.319 \pm .082$, in lots 7–9, $+.539 \pm .069$ and in lots 10–14 $+.572 \pm .048$. For reasons which have been mentioned the latter two groups are much more satisfactory than the group of three miscellaneous lots, 3, 4 and 5. The average in lots 7–9 and 10–14 is $+.560 \pm .039$. The square of this coefficient, .314 indicates that over 30 per cent. of the variation in length of life is caused by heredity, neglecting such heredity as may be due to differences among families 2, 13, 32 and 39.

If we assume that some 10 per cent. of the variation is due to differences in condition, weight and age and over 30 per cent. to heredity, we still have over 50 per cent. of the variation due to unknown causes. From the nature of the case, however, a large amount of accidental variation is to be expected.

RELATIONS BETWEEN RESISTANCE AND OTHER CHARACTERISTICS

It is clear that family 35 is markedly more resistant to tuberculosis than the other inbred families, and that among these, family 2 is somewhat more resistant than families 13, 32 and probably 39. The question arises whether these differences in resistance are related to any of the other characteristics in which these families differ.

We may dismiss color with a few words. Families 32 and 39 produce only animals of the primitive golden agouti color; families 2 and 13 produce only blacks, a color which differs from golden agouti by a single recessive factor; family 35 is composed of yellow agoutis. This color is recessive to golden agouti, depending on an allelomorph of albinism. We can not attribute the high resistance of family 35 to the yellow agouti color since the even more highly resistant crossbreds between family 35 and the other families are all of the golden agouti color also found in the susceptible families 32 and 39.

In all of the families there are varying amounts of white in a piebald pattern and of red or yellow in a tortoise-shell pattern. No influence can be attributed to the amount of white unless it is assumed that an intermediate condition is superior to either extreme. Family 39 has the least white, averaging less than 20 per cent.; families 13 and 32 have the most, averaging over 80 per cent.; while families 2 and 35 are intermediate with about 70 per cent. and 60 per cent. white, respectively. It may be added that the correlation between the amount of white in the coat and length of life in family 35, lots 10–14, was found to be virtually zero. Similarly, family 35 is intermediate between family 39 with least red and family 2 with most red in the colored parts of the coat.

The records in size, fertility and death rate among the inbred families and cross breeding experiments during the year 1919, in which all of these tested animals were born, is given in Table XVI. In this table, the weights and mortality records are corrected for the important effects of size of litter by calculating separately the averages in litters of 1, 2, 3 and 4 and finding an index in which these averages are weighted 1, 3, 3 and 1, respectively. This means practically that all of the records are reduced to the basis of an average size of litter of 2.50.

Because of the method of averaging, the figures are not strictly comparable to those presented in Tables VII, VIII and IX for the animals actually tested. However, it is safe to conclude from a comparison of these tables that the animals tested were a fairly random selection from their respective families and experiments.

It may be noted in passing that the figures in Table XVI give a good illustration of the statements made in regard to the effects of crossing, with the exception of a few records based on inadequate numbers.

TABLE XVI

AVERAGES OF THE CHARACTERISTICS OF GUINEA PIGS BORN IN FIVE INBRED FAMILIES (2, 13, 32, 35 AND 39) AND CERTAIN CROSSBREEDING EXPERIMENTS IN 1919

CO is the first cross between inbred families. In *CA*, the sire is crossbred, dam inbred. *AC* is the reverse of *CA*. *B* is the control stock. The mortality and size characters are indices in which the averages for litters of 1, 2, 3 and 4 are weighted 1, 3, 3 and 1 respectively.

Family or Experiment	Number Young	Per Cent. Born Alive	Per Cent. Raised of Those Born Alive	Per Cent. Raised	Birth Weight (Grams)	Gain per Day to 33 Days (Grams)	Weight at 33 Days (Grams)	Size of Litter	Litters per Year	Young per Year	Young Raised per Year
2	331	80.3	88.9	71.4	76.9	3.40	189.1	2.43	3.82	9.30	6.46
13	259	87.1	85.2	74.2	88.4	4.76	245.4	2.85	3.79	10.79	6.67
32	146	90.3	78.8	71.2	82.2	4.13	218.6	2.25	3.48	7.81	5.30
35	258	80.2	84.7	67.9	88.3	4.57	239.1	2.37	3.68	8.72	5.64
39	72	93.7	80.7	75.6	77.9	3.79	203.1	2.40	2.97	7.13	5.15
Tot. Inbred	1,066	84.0	85.1	71.5	82.8	4.12	218.9	2.47	3.63	8.97	5.96
CO	280	91.1	89.4	81.4	81.5	4.52	230.5	2.55	3.90	9.93	7.87
CA	302	85.8	94.5	81.1	84.3	4.53	233.8	2.72	4.24	11.53	9.20
AC	419	87.7	90.9	79.7	88.5	4.54	238.2	3.27	4.16	13.60	10.78
B	374	90.0	84.9	76.4	90.2	4.94	253.2	2.90	3.76	10.90	7.96

From this table it will be seen that family 35, the most resistant to tuberculosis, held a rather low position among the inbred families in most other respects. It is actually the poorest in mortality among the young, and fourth in size of litter and first in nothing. There was thus no close relation between high resistance to tuberculosis and vigor in other respects in 1919.

However, the rank of a family in a single year is not always a safe indication of its true position genetically in characters in which environmental conditions are of very much more importance than heredity. The rank of the families has been calculated for the periods 1906–1910, 1911–15 and 1916–19, making due corrections for the effects of size of litter. As previously stated, high correlations were found between the ranks in the first two periods in most respects among the 23 inbred families. Table XVII shows the ranks of the 5 surviving families in the second and third period. The reality of the differences among these families is evident. Taking the following 6 characters—percentage born alive, percentage of these raised, birth weight, gain to 33 days, frequency and size of litter—the correlation between the ranks in the two periods is + .83.

TABLE XVII

RANK OF FAMILIES IN RESISTANCE TO TUBERCULOSIS IN 1919, AND RANK IN OTHER CHARACTERISTICS DURING TWO PERIODS, 1911–15 AND 1916–19

Mortality and size characters are corrected for the influence of size of litter and (in 1916–19) for seasonal differences.

Family	Resistance to Tuberculosis	Per Cent. Born Alive	Per Cent. Raised of those Born Alive	Per Cent. Raised	Birth Weight	Gain to 33 Days	Weight at 33 Days	Adult Weight	Size of Litter	Litters per Year	Young per Year	Young Raised per Year
35....	1	3–3	3–1	3–1	2–2	2–2	2–2	2–2	1–2	2–2	1–1	1–1
2....	2	5–5	1–2	4–2	5–5	5–5	5–5	5–4	4–4	1–1	4–2	3–2
13....	3	2–4	2–3	2–4	1–1	1–1	1–1	1–1	2–1	3–4	2–3	2–3
32....	3	4–2	5–5	5–5	3–3	4–3	4–3	4–5	5–5	4–3	5–4	5–4
39....	3	1–1	4–4	1–3	4–4	3–4	3–4	3–3	3–3	5–5	3–5	4–5

The positions of the families agree in the main with those for the single year 1919. The position of family 35, however, is much better in most respects, a point which will be discussed later.

The difficulty of classifying the families in the order of general vigor is shown by this table. Families 2, 13 and 39 present curious combinations of high vigor in certain respects with weakness in others. It is true that there is perfect correlation between the ranks in size of litter and adult weight, but the order in which this places the families, 13, 35, 39, 2 and 32, is far from being the order in frequency of litter or the mortality records. Taken as a whole, family 2 seems to have been rather the easiest family to keep going. Its regularity in producing litters and success in raising the young which are born alive are factors in this, but even more important seems to be another factor, probably correlated with that last named, the longevity of the animals after the matings are made, in which it far surpasses all of the others. Families 13 and 35 have also been relatively easy to maintain. This leaves families 32 and 39 as those most difficult to keep up to a desirable strength.

In spite of the better record of family 35 in the four years, 1916–19, as compared with the single year 1919, there is still no close relation between resistance to tuberculosis and vigor in other respects. In size, in both elements of fertility, and in the percentage of the young born alive, family 35 is still inferior to families which are distinctly more susceptible to tuberculosis. It may, however, be significant that family 35 led in the percentage raised of the young born alive and that family 2, second in resistance, is also second in this respect.

It may also be significant that while family 35 does not stand out in any particular element of vigor, unless in that last named, it stands relatively high in all, and so is the best family in the number of young produced per year by a mating, the product of frequency and size of litter, and is also the best family in the total percentage of the young raised, the product of the percentage born alive and the percentage of these raised. Moreover, family 2 is second in both respects as in resistance. These results suggest that while resistance to tuberculosis is not related to the most important factors which determine the various elements of vigor, it is a contributing factor to a sufficient extent to make the total efficiency of a resistant family higher than that of a susceptible family.

In this connection, the low standing of family 35 during 1919 requires some consideration. The general condition of the stock was much better in 1919 than in any of the three preceding years. The principal cause of the high death rate, small and infrequent litters and slow growth during 1916, 1917 and 1918, especially during the first half of each year, was probably an insufficient supply of green feed during late winter and early spring. Symptoms, such as lameness, swollen and bleeding gums, were noted rather frequently. These were probably indicative of scurvy. A form of pneumonia was also rather common. Whether tuberculosis was present in the stock at this time is not certainly known. It is doubtful, as guinea pigs seldom take the disease unless directly inoculated. However, this may be, it seems probable that family 35 has a special ability to withstand exceptionally adverse conditions. It is not unlikely that this characteristic may be connected directly or indirectly with its resistance to tuberculosis. Under good conditions, on the other hand, there seems to be little if any relation between this form of vigor and apparent vigor in other respects.

CONCLUSIONS

There is little or no relation among guinea pigs between resistance to tuberculosis and sex. The present data indicate a possible superiority of the males, but one which is too slight to be certainly significant.

The data suggest a slightly greater susceptibility among the progeny of very young or very old females but this also is of doubtful significance.

Size of litter, birthweight and rate of gain up to weaning give virtually no indication of the probable length of life after inoculation.

The rate of gain preceding inoculation and the age and weight at that time all together determined less than 7 per cent. of the variation in length of life in a very heterogeneous lot of guinea pigs and less than 2 per cent. in a somewhat more homogeneous lot.

Marked differences in resistance were found among a number of inbred families of guinea pigs.

The high resistance of one of these families was transmitted by each sex to the offspring of each sex in crosses with other inbred families.

In crosses involving this most resistant family, the progeny were superior even to this family itself, indicating not only the dominance of resistance over susceptibility but possibly also the presence of complementary factors among the families.

In crosses among the more susceptible families, the progeny were little, if any, superior to the family of the better parent, indicating dominance but not complementary factors in this case.

Over 30 per cent. of the variation in length of life after inoculation among the crossbreds was determined by the amount of blood from the best inbred family. Allowing 10 per cent. of the variation as due to age, weight and condition, 50 to 60 per cent. remains as due to accidental and unknown causes.

The factors which determine the resistance of a family to tuberculosis are not closely related to the other elements of vigor, including rate of growth and adult weight, frequency and size of litter, the percentage of the young born alive and the percentage of these raised to weaning. There is some evidence that they are contributing factors to a sufficient extent to give the most resistant family a record above the average in each element of vigor and so give it the highest or nearly the highest total efficiency. Even this relation of resistance to other elements of vigor appears to be present only under exceptionally adverse conditions when it may play a direct part in determining the health of the stock.

The results in regard to resistance to tuberculosis are like those for other characteristics as regards the differentiation among families brought out by inbreeding, the improvement resulting from crosses between inbred families and the independence genetically from other elements of vigor.